

REMARKS

Upon entry of the foregoing amendment, claims 1-7 and 10 will remain pending in the application. Claim 11 has been added. The new claim does not introduce new matter, and their entry is respectfully requested.

In the Office Action of October 15, 2008, the Examiner set forth a number of grounds for rejection. These grounds are addressed individually and in detail below.

Claim Rejections Under 35 U.S.C. § 103

Claims 1-5, 7 and 10 stand rejected under 35 U.S.C. §103(a) over Leskovar et al. (hereinafter "Leskovar") (WO 89/09620) for the reasons set forth on pages 2-8 of the Office Action. Claims 1-7 and 10 stand rejected under 35 USC 103(a) over Leskovar in view of Housman et al. (hereinafter "Housman") (US 6,200,754) for the reasons set forth on pages 8-9 of the Office Action. Applicants respectfully traverse the rejections.

The present independent Claim 1 is directed to a pharmaceutical composition for cancer therapy consisting essentially of: a) at least one compound having glutaminase activity; b) at least one antineoplastic agent selected from the group consisting of platinum complexes and anthracyclines; and c) at least one of carrier substances, auxiliary substances, and pharmaceutical injection media.

The Examiner maintained in the Final Office Action that the term "anthracyclines" does not in itself exclude anthracyclines that are conjugated to an antibody. Applicants respectfully disagree. The specification of the present application only discloses anthracyclines, including daunorubicin, doxorubicin. The specification gives no indications, neither explicitly nor implicitly, that anthracyclines include the anthracyclines that are conjugated to an antibody.

It is well established in the patent law that ordinary, simple English words whose meaning is clear and unquestionable, absent any indication that their use in a particular context changes their meaning, are construed to mean exactly what they say. *Chef America, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1372, 69 USPQ2d 1857 (Fed. Cir. 2004)

In this case, the National Cancer Institute, National Institutes of Health of the United States of America, defines “anthracycline” as “a type of antibiotic that comes from certain types of *Streptomyces* bacteria” (Exhibit 1). Similarly, Wikipedia defines “anthracyclines” as “a class of drugs used in cancer chemotherapy derived from *Streptomyces* bacteria (more specifically, *Streptomyces peucetius* var. *caesius*)” (Exhibit 2). Thus, the ordinary meaning of the word “anthracyclines” is clear and unquestionable and should be interpreted as its plain meaning, which clearly excludes antibody-conjugated anthracyclines because an antibody conjugate cannot come from or derive from *Streptomyces* bacteria. Therefore, the antineoplastic agent of instant Claim 1 would not read on an immunoconjugate of anthracycline.

Leskovar only describes a medicament which comprises (1) antibodies or conjugates of antibodies and cytotoxic agents (*i.e.*, component A) and (2) activators of effector cells (*i.e.*, component B). The cytotoxic agents include anthracyclines such as doxorubicin and daunomycin (Leskovar, paragraph [0023]). The conjugates of antibodies include antibodies conjugated to asparaginase or glutaminase (Leskovar, paragraph [0192]).

Leskovar does not teach or suggest using unconjugated anthracyclines in a pharmaceutical composition, as recited in instant Claim 1. In fact, by including activators of effector cells as one of the two key ingredients of the claimed invention, Leskovar **teaches away** from a composition that does not contain activators of effector cells. For this reason alone, instant claim 1 is patentable over Leskovar.

Moreover, Leskovar does not teach or suggest using both anthracycline and glutaminase in the same composition. The Examiner alleges that Leskovar teaches that both the glutaminase conjugate and the anthracycline conjugate are useful to treat tumors and, therefore, it is prima facie obvious to one of ordinary skill in the art to combine the glutaminase conjugate with the anthracycline conjugate into the same composition. Applicants respectfully disagree.

Leskovar discloses a large number of antibody conjugates that can be used to treat cancer (see e.g., paragraphs [0022], [0023], [0140], [0191], and [0192]). Glutaminase conjugate and anthracycline conjugate are two species of anti-tumor conjugates among thousands of anti-tumor conjugates disclosed in Leskovar. It is well established in patent law that the disclosure of a genus does not automatically render a particular species obvious. The Office personnel should consider a number of factors, including the size of the genus, the express teachings, and the predictability of the technology (see, e.g. MPEP 2144.08).

In the present case, Leskovar discloses a huge genus of anti-tumor conjugates and potential combination of these conjugates. The specification of Leskovar does not teach or suggest using a combination of anti-tumor conjugates, nor the particular combination of glutaminase conjugate and anthracycline conjugate. The biotechnology is generally considered an unpredictable art. It is unpredictable that a combination of glutaminase conjugate and anthracycline conjugate would be more effective than each individual conjugate, let alone the combination of unconjugated glutaminase and unconjugated anthracycline.

Furthermore, Leskovar uses the complete different mechanism as the present claimed invention does. The present claimed invention is to first weaken the tumor cells by removing the glutamine, which is important for the development and growth of tumor cells, and then, to treat tumor cells by neoplastic agent. In doing so, any tumor cells which are present at any sites of

the body can be attacked successfully. In contrast, Leskovar pursues a complete different approach, in which specific antibodies are used and suppressor cells in the subject are eliminated and activator cells are activated. The specific attack on suppressor cells by means of antibodies is an essential step in Leskovar (paragraph [0006]) which is substantially different from the administration of glutaminase and antineoplastic agents of the present claimed invention. Therefore, one skilled in the art would not be able to produce the present claimed invention based on Leskovar without undue experimentation.

Thus, Leskovar does not render the present Claim 1 obvious because it does not teach or suggest the combination of unconjugated glutaminase and unconjugated anthracycline.

Houseman does not remedy the deficiency of Leskovar. Houseman is cited for its teachings on mitomycin C and *cis*-platinum. Houseman does not teach or suggest using unconjugated anthracyclines in a pharmaceutical composition, nor does it teach or suggest a composition consisting essentially of a compound having glutaminase activity and unconjugated anthracyclines, as recited in Claim 1 of the instant application.

Accordingly, Applicants respectfully submit that Leskovar and Housman, individually or in combination, do not render Claim 1 obvious because they fail to teach or suggest all the claim limitations. Applicants further submit that Claims 2-7 and 10 are patentable over Leskovar and Housman because they depend from Claim 1, either directly or indirectly. New Claim 11 is patentable over Leskovar and Housman for the same reasons stated above.

In view of the foregoing, Applicants respectfully submit that these grounds of rejection have been obviated and withdrawal of the rejection under 35 U.S.C. §103 is respectfully requested.

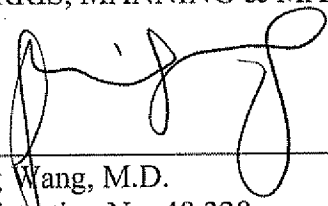
CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to contact Applicants' counsel, Ping Wang, M.D. (Reg. No. 48,328), at 202.842.0217.

Respectfully submitted,

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Attachments:

EXHIBIT 1
EXHIBIT 2